

**INTERSPECIES EMBRYONIC STEM CELL****CLAIMS**

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1. An isolated embryonic stem cell (ES), characterised in that it is an interspecies *Mus musculus* X *Mus spretus* hybrid ES cell.
  2. The ES cell of any of claim 1, characterised in that said interspecies hybrid stem cells  
10 have germ line transmission capability.
  3. The interspecies *Mus musculus* x *Mus spretus* ES cell lines of claim 1 or 2, characterised in that more than 40% of the microsatellites of its DNA are polymorphic in length.
  - 15 4. The interspecies *Mus musculus* x *Mus spretus* ES cell lines of claim 1 or 2, characterised in that more than 70% of the microsatellites of its DNA are polymorphic in length.
  - 20 5. The interspecies *Mus musculus* x *Mus spretus* ES cell lines of claim 1 or 2, characterised in that more than 90% of the microsatellites of its DNA are polymorphic in length.
  - 25 6. The ES cell as in the claims 1 or 5, wherein the *Mus spretus* genomic background is from SPRET/Ei (Spain) Ei *Mus spretus* strain mice.
  7. The ES cell as in the claims 1 or 5, wherein the *Mus musculus* genomic background is from C57BL/6J
  - 30 8. The ES cell as in the claims 1 or 7, characterised in that the interspecies hybrid ES cell are derived from SPRET/Ei *Mus spretus* strain x C57BL6/J *Mus musculus* strain.
  9. A population of the isolated embryonic stem cell (ES) of the claims 1 to 8.
  - 35 10. A pure population of the isolated embryonic stem cell (ES) of the claims 1 to 8.
  11. The use of the interspecies *Mus musculus* x *Mus spretus* hybrid ES cells of the claims 1 to 10 in a method for introducing mutations into the *Mus spretus* genome.
  - 40 12. The use of the interspecies *Mus musculus* x *Mus spretus* hybrid ES cells of the claims 1 to 10 in a method for introducing mutations specifically into *Mus spretus* allele.
  13. The use of the the interspecies *Mus musculus* x *Mus spretus* hybrid ES cells of the claims 1 to 10 in a method for introducing mutations into the *Mus spretus* genome,

said method comprising a) transfection of the interspecies *Mus musculus* x *Mus spretus* hybrid embryonic stem (ES) cells with a gene-targeting construct, which specifically recombines homologously with the *Mus spretus* gene, b) assessing *Mus musculus* x *Mus spretus* hybrid ES cells for homologous recombination, c) generating chimeric mice by blastocyst injection d) assessing germline transmission of the *Mus spretus* genome and e) breeding the chimeric mice, which transmit the *Mus spretus* genome, to homozygosity, in a pure *Mus spretus* background.

14. The use of claims 11 to 13, wherein the mutations are of the groups consisting of, null mutations, point mutations, translocations, inversions or deletions.

15. The use of the interspecies *Mus musculus* x *Mus spretus* hybrid ES cells of the claims 1 to 10 in a method for analysing gene function or identification of quantitative trait loci comprising the generation of radiation induced chromosomal deletion in high polymorphism interspecies hybrid ES cells of *Mus musculus* x *Mus spretus* of the claim 1 to 10.

16. A method for introducing mutations into the *Mus spretus* genome, comprising a) transfection of the interspecies *Mus musculus* x *Mus spretus* hybrid embryonic stem (ES) cells with a gene-targeting construct, which specifically recombines homologously with the *Mus spretus* gene, b) assessing *Mus musculus* x *Mus spretus* hybrid ES cells for homologous recombination, c) generating chimeric mice by blastocyst injection, d) assessing germline transmission of the *Mus spretus* genome and e) breeding the chimeric mice, which transmit the *Mus spretus* genome, to homozygosity, in a pure *Mus spretus* background.

17. The method of claim 16, wherein the mutations are of the groups consisting of, null mutations, point mutations, translocations, inversions or deletions.

18. A method for analysing gene function or identification of quantitative trait loci comprising the generation of radiation induced chromosomal deletion in the interspecies hybrid ES cells of *Mus musculus* x *Mus spretus* of claim 1 to 10.

19. An high-through put analysis system comprising the cell or cell population of any of the claims 1 to 10, for analysing gene function

20. An high-through put analysis system comprising the cell or cell population of any of the claims 1 to 10, for analysing gene function for identification of quantitative trait loci